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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,390	01/22/2004	Koral Embil	EDKO-001	2411

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EXAMINER	
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ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/761,390	EMBIL ET AL.	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16-26 and 29-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,16-26 and 29-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Declaration of amendment, response and declaration of Martin Katz, all dated 6-27-08 is acknowledged.

Claims 1-14, 16-26 and 29-35 are pending in the instant application.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 1, 2, and 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/15726 (submitted on PTO-1449, hereafter WO 26) in view of US 5879716 (Katz).

WO 26 teaches a composition for acne treatment comprising clindamycin and benzoyl peroxide in the form of a kit, separately maintained in different containers (page 9, L 25-35 and Example compositions on pages 11-12). Benzoyl peroxide composition comprises a polymer and both compositions have water and hence meet the claimed limitations. WO 26 fails to state the lipophilicity exclusively, the compositions of two components (table 1) are both water based and do not appear to vary in their hydrophilicity or lipophilicity and teaches adjusting the viscosity of the compositions for better release and activity.

Katz teaches a composition comprising benzoyl peroxide that is impregnated insides porous solid particles or microspheres, prepared by suspension polymerization of monomers (abstract, col. 3, L 65+). Katz teaches that once the microspheres are formed they are impregnated with benzoyl peroxide, introduced as a solution. Katz

further teaches that the composition containing the benzoyl peroxide impregnated microspheres further contain carriers or vehicles and states that when liquid vehicles are used and the impregnant is a solution of an active agent in a solvent, the solvent and the vehicle must be immiscible so that outward diffusion of the active agent will not be accelerated by mutual diffusion between the solvent and vehicle (col. 8, L 1-16). Katz teaches employing appropriate combinations of polar solvents and a non-polar vehicle or vice-versa. Katz also suggests adding other actives such as salicylate etc (col. 7, L 49-54). Accordingly, it would have been obvious for an ordinary skill in the art at the time of the instant invention was made to prepare formulations of benzoyl peroxide and also other actives in combination with other active agents in the formulation of WO by preparing the active agents in an appropriate solvents to impregnate them in a porous polymer and also choose an appropriate carriers such that the release of the active agent is released in appropriate amounts from the porous polymer and at the same time the porous polymer permit the outward diffusion of the active agent at a controlled rate, suggested by Katz. Even though Katz does not explicitly state "lipophilicity", a skilled artisan would have understood that the release of the active agent (in high or low concentration) is related to the diffusion of the active agent out of the polymer and is affected by the carrier.

2. Claims 3-14, 16-26 and 29-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/15726 (submitted on PTO-1449, hereafter WO 26) in view of

US 5879716 (Katz) as applied to claims 1, 2, and 23-24 above, and further in view of Wester et al (hereafter Wester, J. American Academy of Dermatology) and EP 306236 (hereafter EP), both submitted on PTO-1449.

WO 26 described above, fails to teach the claimed microsponge polymer of the instant claims. WO also fails to teach the combination of active agents other than benzoyl peroxide and clindamycin. Katz, discussed above, teaches a porous polymer impregnated with benzoyl peroxide.

Wester teaches controlled release of benzoyl peroxide from a porous microsphere polymeric system for reducing topical irritancy. Wester compared the difference between the release of the above compound from a polymeric composition and non-polymeric composition (freely dispersed drug) and observed that the compound of significantly better absorbed through the skin when released from the former system and also reduced irritation (abstract, lines bridging pages 720-721 and results on page 722-723). The polymeric system of Wester is the same as the instant microsponge.

EP also teaches controlled release of several skin care and hair care active agents such as benzoyl peroxide, salicylic acid, minoxidil etc., from a composition containing a microsponge polymeric system (the same microsponge as that claimed in the instant invention). In particular, EP (as well as Wester) teaches the treatment of acne with benzoyl peroxide. For the various active agents of EP, see pages 2-5, 7, page 12, L 40-45 and examples and on page EP teaches a number of combinations of the active agents.

Thus, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ the microsponge polymeric delivery material of Wester or EP as a polymer in the composition of WO26, either in one or both compartments, because both Wester and EP suggests that the porous polymeric material forms a continuous network open to the exterior particles, permitting outward diffusion of the impregnated active agents in a controlled fashion. Further, EP suggests that the polymer is suitable for a wide variety of active agents and their combinations and hence including any combination of active agents, in the teachings of WO26, that are suitable for acne treatment would have been obvious for a skilled artisan. Further, incorporating more than two active agents in different dispensing containers (in the teachings of WO26), and adjusting the openings or closures, so that the active agents can be dispensed separately would have been obvious from the teachings of EP because EP suggests more than two active ingredients for the same treatment such as acne.

New claims 31-35 directed to the viscosities and the lipophilicity are also rejected under this section because while WO or other references of record fails to teach the specific viscosities claimed, the rejection is based on incorporating micro sponge polymeric delivery material of Wester or EP as a polymer in the composition of WO26 as a polymeric delivery system in place of the polymeric gelling agent of WO and such substitution would naturally result in lower viscosities because the gelling agent of WO is employed for increasing the viscosity of the composition.

Response to Arguments

Applicant's arguments filed 6-27-08 have been fully considered but they are not persuasive.

Applicants argue that each of the pending claims require first and second active ingredient-containing formulations comprised of "water-based carrier bases having substantially the same lipophilicity and that as set out in Paragraphs 7 - 11 of the 1.132 Declaration of Dr. Katz, WO 93/15726 ("WO26") - the primary reference that forms the basis for all of the pending rejections - does not teach or suggest creating a combination formulation made up of two components, where each of the components has substantially the same lipophilicity. It is argued that the declarations of Dr. Katz and Dr. Lochhead conclude that the benzoyl peroxide suspensions taught in WO26 do not have substantially the same lipophilicity as the clindamycin suspensions. The declaration of Dr. Katz states that WO26 does not teach or suggest matching lipophilicity or partition coefficient and only refers to nine (9) non-specific references to the carrier in WO26. It is argued that at most, these references teach a "pharmaceutically acceptable fluid carrier including a gelling agent at a concentration of from 0.1% by weight to 5% by weight" (see WO26 Claim 26) which is aqueous (see WO26 Claim 30). Dr. Katz refers to paragraphs 15 and 16 of the Declaration of Dr. Lochhead to the analysis of the solubility of benzoyl peroxide in different aqueous carriers. It is argued that based on the analysis, the benzoyl peroxide suspensions taught in WO26 Example 5 and WO Example 6 contain, respectively, 11.56 weight % and 7.5 weight % of propylene glycol, which significantly influences the solubility of benzoyl peroxide, and therefore its

lipophilicity in a suspension and hence do not exhibit "substantially the same lipophilicity" as defined in Paragraph 0068 of the instant application. It is argued in Dr. Katz's declaration that a person of ordinary skill in the art understands that carboxyvinyl polymers to be a "polymeric delivery system" as this term is defined in Paragraph [0050] of the instant application. And instead are employed as thickeners.

Applicants' arguments together with the declarations of Dr. Katz and Dr. Lochhead have considered but not found persuasive because firstly, the term "substantially same lipophilicity" is not defined in the instant application and therefore it is not clear what the lipophilicity is being claimed. The declaration of Lochhead provides the solubilities of benzoyl peroxides in various solvents (lone) but fails to show how the solubilities are affected in the compositions of WO, which comprises other components such as propylene glycol. The teachings of WO are in the same field of endeavor i.e., employing effective amounts of benzoyl peroxide and clindamycin that are packaged separately but mixed prior to use. In this regard, each of the examples presented in the instant application contains propylene glycol and applicants have not showed any evidence to support their argument that the presence of components such as propylene glycol in the composition of WO would affect the delivery of benzoyl peroxide or clindamycin or both, upon incorporating the porous polymers of Katz or the polymeric sponge of Wester and/or EP. Thus the arguments are not persuasive because the arguments of counsel cannot take the place of evidence in the record. In the absence of any specific lipophilicity or the definition of the term "substantially same lipophilicity", it would have been within the scope of a skilled artisan at the time of the instant invention

was made to employ the compostions of benzoyl peroxide and clindamycin with the polymers of Katz or Wester and/or EP such that the mixing of the composition does not adversely affect the very purpose of delivering the active agents for their intended purpose. Further, Applicants did not argue the motivation to combine the polymeric systems of Katz or the micro sponge of Wester with the compositions of WO.

Applicants argue that Claims 24 and 29 - 32 each have a further limitation with respect to the viscosity and the declarations of Dr. Katz and Dr. Lochhead conclude that the prior art teachings do not meet the above limitations. It is argued that the office failed to show where the prior art teaches the claimed viscosities. However, as explained in the rejection above, the addition of the polymeric sponge of Wester or EP would reduce the viscosities of the composition of WO. Applicants argue that the cited references do not provide a teaching, suggestion or motivation to replace the carboxyvinyl polymers taught in WO26 with a polymeric delivery system of the type claimed by the Applicants. It is argued that the carboxyvinyl polymers are not "polymeric delivery systems" and Dr. Lochhead provides a similar explanation in Paragraph 11 of his declaration. Applicants argue that the Office Action does not provide a clearly-articulated rationale explaining why a person having ordinary skill in the viewing the cited references would have considered it obvious to modify the product combination benzoyl peroxide / clindamycin taught in W026 by substituting a polymeric delivery system of the type claimed by the Applicants with a carboxyvinyl polymer as taught in WO26. Applicants' arguments are not persuasive because firstly, the term "polymeric

delivery system" is not defined in the instant specification and merely states what is included in the term. Thus, the carboxyvinyl polymers of WO are not excluded by the above claim term. Further, it is clearly set out in the rejection (above) that the motivation to employ the micro sponge polymeric delivery material of Wester or EP as a polymer in the composition of WO26, either in one or both compartments, comes from the teaching of Wester and EP, which suggest that the porous polymeric material forms a continuous network open to the exterior particles, permitting outward diffusion of the impregnated active agents in a controlled fashion. Further, EP suggests that the polymer is suitable for a wide variety of active agents and their combinations.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -5.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lakshmi S Channavajjala/
Primary Examiner,
Art Unit 1611
September 27, 2008